June 20, 2003

Ann P. LeHuray, Ph.D.
Technical Contact
The American Chemistry Council
Rubber and Plastic Additives (RAPA) Panel
1300 Wilson Boulevard
Arlington, VA 22209

Dear Dr. LeHuray:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Zinc Dibutyldithiocarbamate (ZDBC) posted on the ChemRTK HPV Challenge Program Web site on February 5, 2003. I commend The American Chemistry Council Rubber and Plastic Additives (RAPA) Panel for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The American Chemistry Council Rubber and Plastic Additives (RAPA) Panel advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

*-S-*

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc:
W. Penberthy
M. E. Weber

**EPA Comments on Chemical RTK HPV Challenge Submission:**
**Zinc Dibutyldithiocarbamate**

## Summary of EPA Comments

The sponsor, the Rubber and Plastic Additives Panel of the American Chemistry Council, submitted a test plan and robust summaries to EPA for zinc dibutyldithiocarbamate (ZDBC) (CAS No. 136-23-2) dated January 15, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on February 5, 2003. The test plan includes supporting information on the analog, zinc dimethyldithiocarbamate (ZDMC) (CAS No. 137-30-4).

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. Adequate data are available for all endpoints for the purposes of the HPV Challenge Program except vapor pressure, partition coefficient, water solubility and biodegradation. The submitter needs to provide additional data for these endpoints.

2. Health Effects. Adequate data are available for all endpoints except reproductive and developmental toxicity for the purposes of the HPV Challenge Program. The submitter needs to conduct a combined reproductive and developmental toxicity screening test to adequately address these endpoints.

3. Ecological Effects. EPA reserves judgment on the data adequacy of the three ecological effects endpoints. The submitter needs to provide additional information in the robust summaries. Also, a chronic toxicity study in daphnia will be needed if the measured log $K_{OW}$ is $\geq$4.2.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

## EPA Comments on the Zinc Dibutyldithiocarbamate Challenge Submission

### Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility).

Adequate data are available for melting point and boiling point for the purposes of the HPV Challenge Program.

For several endpoints, the submitter provided an estimated value using EPIWIN. However, this software was not designed to estimate values for organometallics, and so is not appropriate for this chemical. Furthermore, for most of these endpoints, measured values are generally needed.

*Vapor Pressure.* The submitter provided an estimated vapor pressure of $5.8 \times 10^{-11}$ mm Hg. The vapor pressure of the analog ZDMC was reported in the scientific literature as "practically zero" (Hartley and Kidd, 1987) and an extrapolated value of $< 7.5 \times 10^{-9}$ mm Hg was found (Tomlin, 1994). Metal salts such as these zinc complexes would be expected to have a low vapor pressure and these data support the EPIWIN estimate in showing that the test substance is not a volatile chemical. The submitter needs to submit in robust summary format the data cited above or conduct a vapor pressure study using the OECD TG 104 series.

*Partition Coefficient.* The submitter provided an estimated value. EPA recommends that the submitter conduct a measured partition coefficient study using OECD TG 117.

*Water Solubility*. The submitter provided an estimated value. EPA guidelines require measured values for water solubilities >1 mg/L. In addition, the estimated value does not compare favorably with the water solubility (>1,000 mg/L) that the submitter stated was found in the acute fish toxicity studies. Therefore, the submitter needs to conduct a water solubility study using OECD TG 105.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Adequate data are available for photodegradation, stability in water and fugacity for the purposes of the HPV Challenge Program.

*Biodegradation*. The submitter provided a robust summary of an anaerobic biodegradation study on the analog ZDMC. Because the study was conducted under anaerobic conditions and tested inherent biodegradation (adapted inoculum), it provides little insight into the ability of either chemical to pass a ready biodegradation test. Therefore, a ready biodegradation study needs to be conducted on ZDBC using the OECD TG 301 series.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for all endpoints except reproductive and developmental toxicity for the purposes of the HPV Challenge Program. All submitted health effects data are on ZDBC.

*Reproductive Toxicity*. The reproductive toxicity endpoint is not adequately addressed by the one-generation reproductive toxicity study because the study has several deficiencies, is taken from a secondary literature source, and has a reliability code of 4 (reliability could not be determined—secondary source).

Although not included in the test plan, evaluation of organ weights and histopathology of male and female reproductive organs from the submitted 17-week repeated-dose toxicity study could satisfy the reproductive toxicity endpoint, if an adequate developmental toxicity study is available. However, the submitted developmental toxicity study is inadequate (see below).

*Developmental Toxicity.* The submitted developmental toxicity study is not adequate because the exposure route, subcutaneous injection, is not an appropriate exposure route and the highest dose tested did not elicit maternal toxicity.

EPA recommends that the submitter conduct a combined reproductive and developmental toxicity screening test using OECD TG 421 to address these endpoints.

Ecological Effects (fish, invertebrates, and algae).

The adequacy of the fish, aquatic invertebrate and algal endpoints cannot be determined without additional details in the robust summaries. Also, due to the large difference in the reported toxicities to fish and daphnia, a full copy of the rainbow trout study would allow EPA to evaluate data adequacy more completely. Moreover, because the data submitted for the algal toxicity endpoint were on the analog ZDMP, EPA reserves judgment on data adequacy pending the submission of results from a measured water solubility study and an octanol water partition coefficient study. Information on these two endpoints will demonstrate the adequacy of the analog for this endpoint.

*Chronic Toxicity*. No chronic aquatic toxicity data were submitted. If the measured log $K_{OW}$ is $\geq$4.2, chronic effects in aquatic organisms may occur and testing to obtain chronic toxicity data on aquatic invertebrates will be needed.

## Specific Comments on the Robust Summaries

Environmental Fate

*Fugacity*. The submitter needs to provide the input parameter values for the fugacity modeling.

Ecological Effects.

*Fish and Invertebrates.* The submitted robust summaries did not provide sufficient detail to allow independent evaluation of the adequacy of these studies. Details missing from the summaries include, number and size of test groups, concentrations tested, concentration of solvent used to facilitate dissolution, mortality at each concentration and in the control group, change in pH over time, and statistical methods. Dissolved oxygen and pH values were determined throughout the study; however, values were not included in the robust summaries. While dissolved oxygen and pH were reportedly within acceptable limits, the change in pH over time is particularly important since nominal concentrations were used and changes in pH over time would provide insight into changing concentrations of test substance during the test period. The submitter needs to provide the missing study details.

*Algae.* Sufficient detail was not included in the robust summary to allow for an independent evaluation of study adequacy. Details missing from the summary for an analog of the submitted substance include test substance purity, concentrations tested, biomass at the start and end of the study, use and response of controls, water chemistry parameters (including change in pH over time), use of a solvent to facilitate dissolution of the test substance (or aqueous solubility of the test substance to show that concentrations above the solubility limit were not tested), statistical methods, and interval between the addition of test chemical and the introduction of test organisms. The submitter needs to provide the missing study details.

## Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

## References

Harley, D., H. Kidd (eds.) 1987. The Agrochemicals Handbook. 2nd ed. Lechworth, Herts, England: The Royal Society of Chemistry.

Tomlin, Clive. 1994. The Pesticide Manual. A World Compendium. Incorporating "The Agrochemicals Handbook". 10th ed. Bath, UK: The Bath Press.